## FEB 1 9 2004 SUPERIOR NO. 1

SEQUENCE LISTING KUMAGAI, Izumi et al. <120> NOVEL DIABODY-TYPE BISPECIFIC ANTIBODY <130> 4600-0106P <140> US 10/642,284 <141> 2003-08-18 <150> JP 2003-038643 <151> 2003-02-17 <160> 40 <170> PatentIn version 3.1 <210> 1 <211> 33 <212> DNA <213> Artificial Sequence <220> <223> A NcoI-5H back primer <400> 1 nnnccatggc ccaggtccag ctgcagcagt ctg 33 <210> 2 <211> 28 <212> DNA <213> Artificial Sequence <220> <223> B 5H-EagI forward primer <400> 2 nnncggccga ggagactgtg agagtggt 28 <210> 3 <211> 26 <212> DNA <213> Artificial Sequence <220> <223> C EcoRV-5L back primer <400> 3 nnngatatcc taatgaccca atctcc 26

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nnnccatggc ccaggtgcaa ctggttcaga gc
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nnncggccga gctcacggta accagcgta
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<223> I NcoI-hOH back primer
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<223> J hOH-EagI forward primer
<400> 10
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nnncggccga gctaacggtc acc
<210> 11
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<212> DNA
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<223> K EcoRV-h5L back primer
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nnngatatcg tgatgaccca gagccc
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<400> 13
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gcctggaatg gattggtaac atttatc
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gataaatgtt accaatccat tccaggc
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tattactgca cgcgcagtgg c
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gccactgcgc gtgcagtaat a
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atttaagaac aaagtgacca tgacggttga taccagca 38
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gcctcaggcg atacctttac g
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<223> T h5H-Y27D(-)
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                                    21
cgtaaaggta tcgcctgagg c
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<212> DNA
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<223> U h5H-M69LT73R(+)
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caaagtgacc ctgacggttg atcgcagcat ttcga 35
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<212> DNA
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<223> V h5H-M69LT73R(-)
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tcgaaatgct gcgatcaacc gtcagggtca ctttg 35
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<212> DNA
<213> Artificial Sequence
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<223> X h5H-I75SS76RA78V(-)
<400> 24
ttccatatag accgtgcgac tgctggtatc
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<212> DNA
<213> Mouse
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<222> (1)..(354)
<223>
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cag gtc cag ctg cag cag tct ggg tct gag atg gcg agg cct gga gct
                                                                       48
Gln Val Gln Leu Gln Gln Ser Gly Ser Glu Met Ala Arg Pro Gly Ala
                                    10
tca gtg aag ctg ccc tgc aag gct tct ggc gac aca ttc acc agt tac
                                                                       96
Ser Val Lys Leu Pro Cys Lys Ala Ser Gly Asp Thr Phe Thr Ser Tyr
                                                                      144
tgg atg cac tgg gtg aag cag agg cat gga cat ggc cct gag tgg atc
Trp Met His Trp Val Lys Gln Arg His Gly His Gly Pro Glu Trp Ile
        35
                                                                      192
gga aat att tat cca ggt agt ggt ggt act aac tac gct gag aag ttc
Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
    50
aag aac aag gtc act ctg act gta gac agg tcc tcc cgc aca gtc tac
                                                                      240
Lys Asn Lys Val Thr Leu Thr Val Asp Arg Ser Ser Arg Thr Val Tyr
65
                    70
                                        75
                                                             80
                                                                      288
atg cac ctc agc agg ctg aca tct gag gac tct gcg gtc tat tat tgt
Met His Leu Ser Arg Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85
                                    90
                                                         95
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			ggg Gly 100										336
			gtc Val										354
<210 <211 <212 <213	!> 3 !> [	26 342 DNA Mouse	è										
<220 <221 <222 <223	> ( 2> (	CDS (1)	. (342	2)									
_	att		atg Met								-		 48
_		_	tcc Ser 20			_	_	_	_		_		96
			acc Thr					_					144
	_		ctg Leu				_	-	_			-	192
_			agt Ser		_				_			_	240
			gag Glu										288
			cct Pro 100										336
cgt Arg													342
		_											

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<220>
<221> CDS
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cag gtg caa ctg gtg cag agc ggc ggt ggc gtt gtg cag ccg ggc cgc
                                                                       48
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
age etg ege etg tet tge aaa geg age gge tat ace ttt acg ege tat
                                                                       96
Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
acc atg cat tgg gtg cgc cag gcg ccg ggc aaa ggt ctg gaa tgg att
                                                                      144
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
                            40
ggc tat att aac ccg tct cgc ggc tat acc aac tat aat caq aaa gtq
                                                                      192
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val
                        55
aaa gat cgc ttt acc att agc cgc gat aac tct aaa aac acc gcg ttt
                                                                      240
Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Phe
65
                    70
ctg cag atg gat agc ctg cgc ccg gaa gat acc ggc gtg tat ttt tgc
                                                                      288
Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
                85
gcg cgc tac tat gat gac cat tat agc ctg gat tat tgg ggc cag ggc
                                                                      336
Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
            100
acc ccg gtg acc gtt agc tcg
                                                                      357
Thr Pro Val Thr Val Ser Ser
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<210> 28
<211> 324
<212> DNA
<213> Artificial Sequence
<220>
<221> CDS
<222>
      (1)..(324)
<223> Chimeric Sequence (hOL)
<400> 28
gat atc cag atg acc cag agc ccg agc tct ctg agc gcg agc gtg ggc
                                                                       48
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
gat ege gtg ace att acg tge age geg tet age tet gtg age tat atg
                                                                       96
Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
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20 25 30

Asn Trp Tyr 35	cag caa Gln Gln											144
gat acc agc Asp Thr Ser 50												192
ggt agc ggc Gly Ser Gly 65												240
gat att gcg Asp Ile Ala												288
ttt ggc cag Phe Gly Gln												324
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<220> <221> CDS												
<222> (1).	.(354) eric Seq	uence (	15H)									
<222> (1).	eric Seq ctg gtt	cag ag	ggc :	gcg Ala	gaa Glu 10	gtg Val	aaa Lys	aag Lys	ccg Pro	ggc Gly 15	gcg Ala	48
<222> (1). <223> Chim <400> 29 cag gtg caa Gln Val Gln	eric Seq ctg gtt Leu Val 5 gtg agc	cag age Gln Se	ggc Gly	Ala	Glu 10 ggc	Val tat	Lys	Lys	Pro acg	Gly 15 agc	Ala	48
<222> (1). <223> Chim <400> 29 cag gtg caa Gln Val Gln 1 tcg gtt aaa	ctg gtt Leu Val 5 gtg agc Val Ser 20 tgg gtg	cag age Gln Set tgc aaa Cys Ly:	ggc ggc Gly a gcc Ala	Ala tca Ser 25	Glu 10 ggc Gly ggt	Val tat Tyr	Lys acc Thr	Lys ttt Phe ctg	Pro acg Thr 30 gaa	Gly 15 agc Ser	Ala tac Tyr atg	
<222> (1). <223> Chim <400> 29 cag gtg caa Gln Val Gln 1 tcg gtt aaa Ser Val Lys tgg atg cat Trp Met His	ctg gtt Leu Val 5 gtg agc Val Ser 20 tgg gtg Trp Val	cag age Gln Se:  tgc aaa Cys Lya  cgc cae Arg Gla	g ggc Gly a gcc Ala g gcc Ala 40	tca ser 25 ccg Pro	Glu 10 ggc Gly ggt Gly	tat Tyr cag Gln	Lys acc Thr ggc Gly	ttt Phe ctg Leu 45	Pro acg Thr 30 gaa Glu	Gly 15 agc Ser tgg Trp	Ala tac Tyr atg Met	96
<pre>&lt;222&gt; (1). &lt;223&gt; Chim  &lt;400&gt; 29 cag gtg caa Gln Val Gln 1  tcg gtt aaa Ser Val Lys  tgg atg cat Trp Met His</pre>	ctg gtt Leu Val 5 gtg agc Val Ser 20 tgg gtg Trp Val tat ccg Tyr Pro gtg acc	tgc aaa Cys Lys cgc caa Arg Gli ggc age Gly Ses 55	g ggc Gly a gcc Ala g gcc Ala 40 ggt Gly	tca Ser 25 ccg Pro ggc Gly	Glu 10 ggc Gly ggt Gly acc Thr	tat Tyr cag Gln aac Asn	Lys acc Thr ggc Gly tat Tyr 60 att	ttt Phe ctg Leu 45 gcg Ala	Pro acg Thr 30 gaa Glu gaa Glu	Gly 15 agc Ser tgg Trp aaa Lys	Ala tac Tyr atg Met ttt Phe	96 144

gcg cgc agt ggc Ala Arg Ser Gly 100 ctg gtt acc gtg Leu Val Thr Val	Gly Pro Tyr		
<220>	al Sequence		
<pre>&lt;221&gt; CDS &lt;222&gt; (1)(34 &lt;223&gt; Chimeric</pre>	2) : Sequence (h5	5L)	
<400> 30 gat att gtg atg Asp Ile Val Met 1			
gaa ccg gcg tcg Glu Pro Ala Ser 20			
aac ggc att acc Asn Gly Ile Thr 35			
ccg cag ctg tta Pro Gln Leu Leu 50			 
gat cgc ttt tcg Asp Arg Phe Ser 65	Gly Ser Gly	Ser Gly Thr As	Lys Ile
agc cgc gtg gaa Ser Arg Val Glu			
agc cat atc ccg Ser His Ile Pro 100	Pro Thr Phe		
cgc gcg Arg Ala			342

<210> 31 <211> 118 <212> PRT

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<220>
<223> Chimeric Sequence (h5H-m01)
<400> 31
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20
                                25
Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
Lys Asn Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
                    70
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85
                                    90
Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
            100
Leu Val Thr Val Ser Ser
        115
<210> 32
<211> 118
<212> PRT
<213> Artificial Sequence
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<223> Chimeric Sequence (h5H-m02)
<400> 32
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20
                                25
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<213> Artificial Sequence

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe 50 60

Lys Asn Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Thr 85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr 100 105 110

Leu Val Thr Val Ser Ser 115

<210> 33

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric Sequence (h5H-m03)

<400> 33

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met 35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe 50 55 60

Lys Asn Lys Val Thr Met Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr 100 105 110

Leu Val Thr Val Ser Ser 115

<210> 34

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric Sequence (h5H-m04)

<400> 34

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe 50 60

Lys Asn Lys Val Thr Met Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser 115

<210> 35

<211> 118

<212> PRT

<213> Artificial Sequence

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<223> Chimeric Sequence (h5H-m05)
<400> 35
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Asp Thr Phe Thr Ser Tyr
Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
                            40
Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
Lys Asn Lys Val Thr Met Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
                    70
                                        75
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85
                                    90
                                                        95
Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
            100
Leu Val Thr Val Ser Ser
       115
<210> 36
<211> 118
<212> PRT
<213> Artificial Sequence
<223> Chimeric Sequence (h5H-m06)
<400> 36
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr

30

20

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe 50 55 60

Lys Asn Lys Val Thr Met Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Thr 85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr 100 105 110

Leu Val Thr Val Ser Ser 115

<210> 37

<211> 118

<212> PRT

<213> Artificial Sequence

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<223> Chimeric Sequence (h5H-m07)

<400> 37

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met 35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe 50 55 60

Lys Asn Lys Val Thr Leu Thr Val Asp Arg Ser Ile Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

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Leu Val Thr Val Ser Ser
        115
<210> 38
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<223> Chimeric Sequence (h5H-m08)
<400> 38
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
                                    10
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
                                25
            20
Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35
                            40
Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
    50
                        55
Lys Asn Lys Val Thr Leu Thr Val Asp Arg Ser Ile Ser Thr Ala Tyr
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
                                105
Leu Val Thr Val Ser Ser
        115
<210> 39
<211> 118
<212> PRT
<213> Artificial Sequence
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<223> Chimeric Sequence (h5H-m09)
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<400> 39

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe 50 60

Lys Asn Lys Val Thr Leu Thr Val Asp Arg Ser Ile Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Thr 85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr 100 105 110

Leu Val Thr Val Ser Ser 115

<210> 40

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric Sequence (h5H-m10)

<400> 40

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe 50 60

Lys Asn Lys Val Thr Met Thr Val Asp Thr Ser Ser Arg Thr Val Tyr 65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Thr 85 90 95

Leu Val Thr Val Ser Ser 115